

-continued

(Nde/Eco)

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Met Lys Ile Lys Thr Gly Ala Arg Ile Leu Ala Leu Ser Ala Leu Thr
 1 5 10 15

Thr Met Met Phe Ser Ala Ser Ala Leu Ala
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<210> SEQ ID NO 43

<211> LENGTH: 69

<212> TYPE: DNA

<213> ORGANISM: Artificial

<220> FEATURE:

<223> OTHER INFORMATION: FGF21 secretion constructs, cloned into pVK7ara (Nde/Eco)

<400> SEQUENCE: 43

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gcctatgca 69

<210> SEQ ID NO 44

<211> LENGTH: 23

<212> TYPE: PRT

<213> ORGANISM: Artificial

<220> FEATURE:

<223> OTHER INFORMATION: FGF21 secretion constructs, cloned into pVK7ara (Nde/Eco)

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Met Lys Lys Asn Ile Ala Phe Leu Leu Ala Ser Met Phe Val Phe Ser
 1 5 10 15

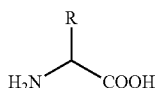
Ile Ala Thr Asn Ala Tyr Ala
 20

What is claimed is:

1. A modified FGF-21 polypeptide comprising a non-naturally encoded amino acid, wherein:

(a) the modified FGF-21 polypeptide comprises a sequence at least 90% identical to SEQ ID NO: 1 fused to an N-terminal methionine, SEQ ID NO: 2, SEQ ID NO: 3, SEQ ID NO: 4, SEQ ID NO: 5 fused to an N-terminal methionine, SEQ ID NO: 6, or SEQ ID NO: 7;

(b) the non-naturally encoded amino acid has the structure:



wherein the R group is any substituent other than the side chain found in alanine, arginine, asparagine, aspartic acid, cysteine, glutamine, glutamic acid, glycine, histidine, isoleucine, leucine, lysine, methionine, phenylalanine, proline, serine, threonine, tryptophan, tyrosine, valine, pyrrolysine, or selenocysteine;

(c) the modified FGF-21 polypeptide contains a substitution of an amino acid with the non-naturally encoded amino acid at position 108 of SEQ ID NO: 1 or the corresponding amino acid position in SEQ ID NO: 2, SEQ ID NO: 3, SEQ ID NO: 4, SEQ ID NO: 5, SEQ ID NO: 6, or SEQ ID NO: 7;

(d) the modified FGF-21 polypeptide maintains the biological activity of human FGF-21 polypeptides; and

(e) the non-naturally encoded amino acid is linked to a linker, polymer, and/or biologically active molecule.

2. The modified FGF-21 polypeptide of claim 1, wherein the non-naturally encoded amino acid is a phenylalanine derivative or is para-acetyl-L-phenylalanine.

3. The modified FGF-21 polypeptide of claim 1, wherein the non-naturally encoded amino acid comprises a first functional group and the linker, polymer, or biologically active molecule comprises a second functional group, wherein the first functional group and second functional group are not identical and each comprise a carbonyl group, an aminooxy group, a hydrazide group, a hydrazine group, a semicarbazide group, an azide group, or an alkyne group.

4. The modified FGF-21 polypeptide of claim 3, wherein the first functional group on the non-naturally encoded amino acid is a carbonyl moiety and the second functional group on the linker, polymer, or biologically active molecule is an aminooxy moiety, and the resultant covalent linkage created by the reaction of the first and second functional groups is an oxime linkage.

5. The modified FGF-21 polypeptide of claim 1, wherein the polymer comprises a poly(ethylene glycol).

6. The modified FGF-21 polypeptide of claim 5, wherein said poly(ethylene glycol) has an average molecular weight of between about 0.1 kDa and about 100 kDa.

7. The modified FGF-21 polypeptide of claim 6, wherein said poly(ethylene glycol) has an average molecular weight of about 30 kDa.